

Amendments to the Claims

1.-9. (Canceled)

10. (currently amended) A method for treating female sexual arousal disorder comprising:

orally administering to a female subject in need thereof, an effective amount of an estrogen agonist / antagonist, and further comprising orally co-administering a cyclic guanosine 3',5'-monophosphate elevator.

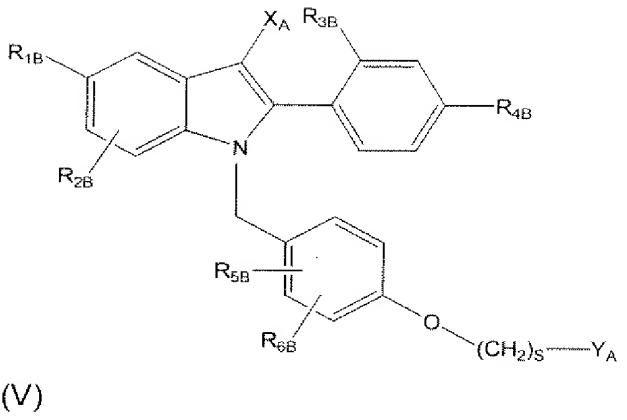
11. (previously presented) The method of claim 10 wherein said cyclic guanosine 3',5'-monophosphate elevator is a PDE_V phosphodiesterase inhibitor.

12. (previously presented) The method of claim 11 wherein the PDE_V phosphodiesterase inhibitor is 1-[[3-(6,7-dihydro-1-methyl-7-oxo-3-propyl-1H-pyrazolo[4,3-d]pyrimidin-5-yl)-4-ethoxy-phenyl]sufonyl]-4-methylpiperazine citrate salt.

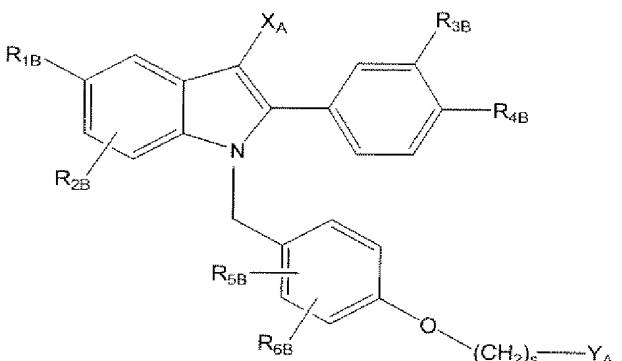
Claims 13.-39. (canceled)

40. (previously presented) The method of claim 10 wherein said estrogen agonist / antagonist is selected from the group consisting of tamoxifen, 4-hydroxy tamoxifen, raloxifene, toremifene, centchroman, idoxifene, 6-(4-hydroxy-phenyl)-5-[4-(2-piperidin-1-yl-ethoxy)-benzyl]-naphthalen-2-ol, {4-[2-(2-aza-bicyclo[2.2.1]hept-2-yl)-ethoxy]-phenyl}-[6-hydroxy-2-(4-hydroxy-phenyl)-benzo[b]thiophen-3-yl]-methanone, EM-652, EM-800, GW 5638, GW 7604, or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt, or prodrug thereof.

41. (previously presented) The method of claim 10 wherein said estrogen agonist / antagonist is a compound selected from the formulas V or VI:



(V)



(VI)

wherein:

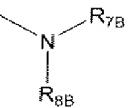
R_{1B} is selected from H, OH, -O-C(O)-C₁-C₁₂ alkyl (straight chain or branched), -O-C₁-C₁₂ alkyl (straight chain or branched or cyclic), or halogens or C₁-C₄ halogenated ethers,

R_{2B}, R_{3B}, R_{4B}, R_{5B}, and R_{6B} are independently selected from H, OH, -O-C(O)-C₁-C₁₂ (straight chain or branched), -O-C₁-C₁₂ (straight chain or branched or cyclic), halogens, or C₁-C₄ halogenated ethers, cyano, C₁-C₆ alkyl (straight chain or branched), or trifluoromethyl, with the proviso that, when R_{1B} is H, R_{2B} is not OH;

X_A is selected from H, C₁-C₆ alkyl, cyano, nitro, trifluoromethyl, and halogen;

s is 2 or 3;

Y_A is the moiety:



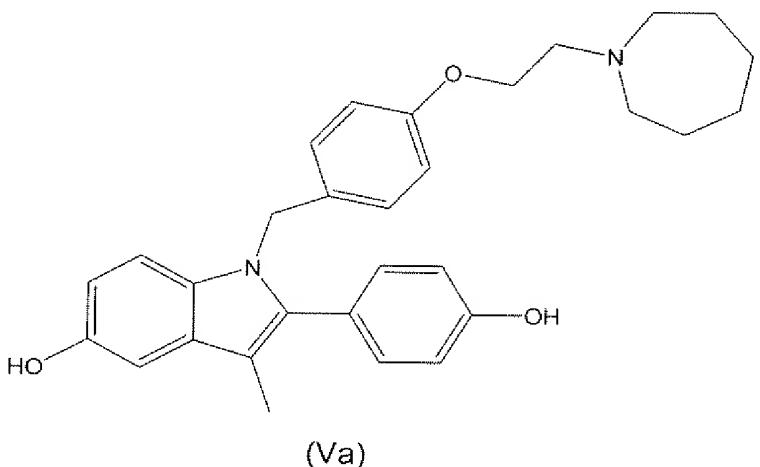
wherein:

- a) R_{7B} and R_{8B} are independently selected from the group of H, C₁-C₆ alkyl, or phenyl optionally substituted by CN, C₁-C₆ alkyl (straight chain or branched), C₁-C₆ alkoxy (straight chain or branched), halogen, -OH, -CF₃, or -OCF₃; or
- b) R_{7B} and R_{8B} are concatenated to form a five-membered saturated heterocycle containing one nitrogen heteroatom, the heterocycle being optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo, C₁-C₄ alkyl, trihalomethyl, C₁-C₄ alkoxy, trihalomethoxy, C₁-C₄ acyloxy, C₁-C₄ alkylthio, C₁-C₄ alkylsulfinyl, C₁-C₄ alkylsulfonyl, hydroxy (C₁-C₄)alkyl, -CO₂H, -CN, -CONHR_{1B}, -NH₂, -NH(C₁-C₄ alkyl), -N(C₁-C₄ alkyl)₂, -NHSO₂R_{1B}, -NHCOR_{1B}, -NO₂, or phenyl optionally substituted with 1-3 (C₁-C₄)alkyl; or
- c) R_{7B} and R_{8B} are concatenated to form a six-membered saturated heterocycle containing one nitrogen heteroatom, the heterocycle being optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo, C₁-C₄ alkyl, trihalomethyl, C₁-C₄ alkoxy, trihalomethoxy, C₁-C₄ acyloxy, C₁-C₄ alkylthio, C₁-C₄ alkylsulfinyl, C₁-C₄ alkylsulfonyl, hydroxy (C₁-C₄)alkyl, -CO₂H, -CN, -CONHR_{1B}, -NH₂, -NH(C₁-C₄ alkyl), -N(C₁-C₄ alkyl)₂, -NHSO₂R_{1B}, -NHCOR_{1B}, -NO₂, or phenyl optionally substituted with 1-3 (C₁-C₄)alkyl; or
- d) R_{7B} and R_{8B} are concatenated to form a seven-membered saturated heterocycle containing one nitrogen heteroatom, the heterocycle being optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo, C₁-C₄ alkyl, trihalomethyl, C₁-C₄ alkoxy, trihalomethoxy, C₁-C₄ acyloxy, C₁-C₄ alkylthio, C₁-C₄ alkylsulfinyl, C₁-C₄ alkylsulfonyl, hydroxy (C₁-C₄)alkyl, -CO₂H, -CN, -CONHR_{1B}, -NH₂, -NH(C₁-C₄ alkyl), -N(C₁-C₄ alkyl)₂, -NHSO₂R_{1B}, -NHCOR_{1B}, -NO₂, or phenyl optionally substituted with 1-3 (C₁-C₄)alkyl; or

e) R_{7B} and R_{8B} are concatenated to form an eight-membered saturated heterocycle containing one nitrogen heteroatom, the heterocycle being optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo, C_1 - C_4 alkyl, trihalomethyl, C_1 - C_4 alkoxy, trihalomethoxy, C_1 - C_4 acyloxy, C_1 - C_4 alkylthio, C_1 - C_4 alkylsulfinyl, C_1 - C_4 alkylsulfonyl, hydroxy (C_1 - C_4)alkyl, $-CO_2H$, $-CN$, $-CONHR_{1B}$, $-NH_2$, $-NH(C_1$ - C_4 alkyl), $-N(C_1$ - C_4 alkyl)₂, $-NHSO_2R_{1B}$, $-NHCOR_{1B}$, $-NO_2$, or phenyl optionally substituted with 1-3 (C_1 - C_4)alkyl; or

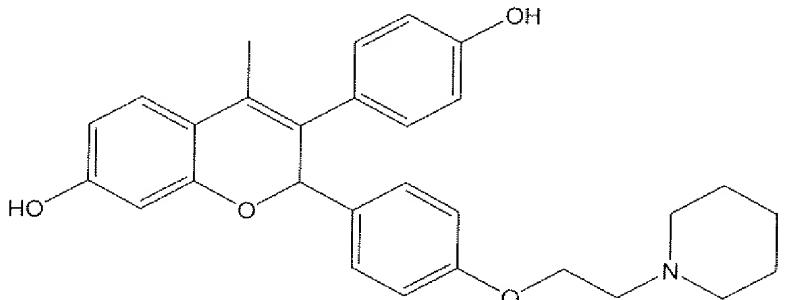
f) R_{7B} and R_{8B} are concatenated to form a saturated bicyclic heterocycle containing from 6-12 carbon atoms either bridged or fused and containing one nitrogen heteroatom, the heterocycle being optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo, C_1 - C_4 alkyl, trihalomethyl, C_1 - C_4 alkoxy, trihalomethoxy, C_1 - C_4 acyloxy, C_1 - C_4 alkylthio, C_1 - C_4 alkylsulfinyl, C_1 - C_4 alkylsulfonyl, hydroxy (C_1 - C_4)alkyl, $-CO_2H$, $-CN$, $-CONHR_{1B}$, $-NH_2$, $-NH(C_1$ - C_4 alkyl), $-N(C_1$ - C_4 alkyl)₂, $-NHSO_2R_{1B}$, $-NHCOR_{1B}$, $-NO_2$, or phenyl optionally substituted with 1-3 (C_1 - C_4)alkyl; or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt or prodrug thereof.

42. (previously presented) The method of claim 41 wherein said estrogen agonist / antagonist is the compound, TSE-424, of formula Va below:



or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt or prodrug thereof.

43. (previously presented) The method of claim 10 wherein said estrogen agonist / antagonist is EM-652 of formula III below or is EM-800 of formula IV below:



orally administering to a female subject in need thereof, an effective amount of (-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt, or a prodrug thereof and further comprising orally co-administering an effective amount of a cyclic guanosine 3',5'-monophosphate elevator.

47. (previously presented) The method of claim 46 wherein the cyclic guanosine 3',5'-monophosphate elevator is a PDE_v phosphodiesterase inhibitor.

48. (previously presented) The method of claim 47 wherein the PDE_v phosphodiesterase inhibitor is 1-[[3-(6,7-dihydro-1-methyl-7-oxo-3-propyl-1H-pyrazolo[4,3-d]pyrimidin-5-yl)-4-ethoxy-phenyl]sufonyl]-4-methylpiperazine citrate salt.

49. (canceled)

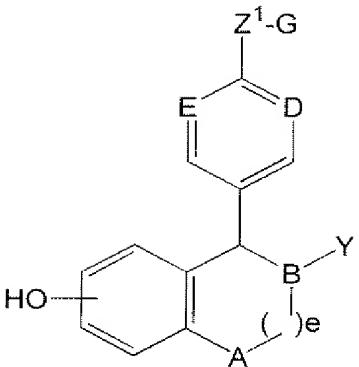
50. (previously presented) The method of claim 46, 47 or 48 wherein (-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol, D-tartrate salt is administered.

51. (previously presented) The method of claim 48 wherein the female subject is pre-menopausal.

52. (previously presented) The method of claim 46 wherein the female subject is postmenopausal.

53. (previously presented) The method of claim 46 wherein the female subject is pre-menopausal.

54. (previously presented) The method of claim 10 wherein the estrogen agonist/antagonist is a compound of formula (I):



(I)

wherein:

A is selected from CH_2 and NR ;

B, D and E are independently selected from CH and N;

Y is

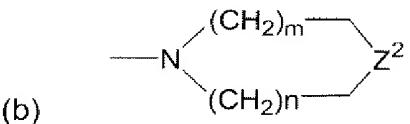
- (a) phenyl, optionally substituted with 1-3 substituents independently selected from R^4 ;
- (b) naphthyl, optionally substituted with 1-3 substituents independently selected from R^4 ;
- (c) $\text{C}_3\text{-C}_8$ cycloalkyl, optionally substituted with 1-2 substituents independently selected from R^4 ;
- (d) $\text{C}_3\text{-C}_8$ cycloalkenyl, optionally substituted with 1-2 substituents independently selected from R^4 ;
- (e) a five membered heterocycle containing up to two heteroatoms selected from the group consisting of $-\text{O}-$, $-\text{NR}^2-$ and $-\text{S}(\text{O})_n-$, optionally substituted with 1-3 substituents independently selected from R^4 ;
- (f) a six membered heterocycle containing up to two heteroatoms selected from the group consisting of $-\text{O}-$, $-\text{NR}^2-$ and $-\text{S}(\text{O})_n-$ optionally substituted with 1-3 substituents independently selected from R^4 ; or
- (g) a bicyclic ring system consisting of a five or six membered heterocyclic ring fused to a phenyl ring, said heterocyclic ring containing up to two heteroatoms selected from the group consisting of $-\text{O}-$, $-\text{NR}^2-$ and $-\text{S}(\text{O})_n-$, optionally substituted with 1-3 substituents independently selected from R^4 ;

Z^1 is

- (a) $-(CH_2)_p W(CH_2)_q-$;
- (b) $-O(CH_2)_p CR^5R^6-$;
- (c) $-O(CH_2)_p W(CH_2)_q-$;
- (d) $-OCHR^2CHR^3-$; or
- (e) $-SCHR^2CHR^3-$;

G is

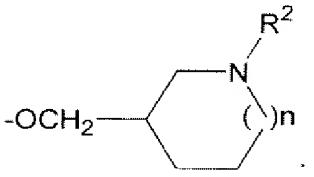
- (a) $-NR^7R^8-$;



wherein n is 0, 1 or 2; m is 1, 2 or 3; Z² is -NH-, -O-, -S-, or -CH₂-;

optionally fused on adjacent carbon atoms with one or two phenyl rings and, optionally independently substituted on carbon with one to three substituents and, optionally, independently on nitrogen with a chemically suitable substituent selected from R⁴; or

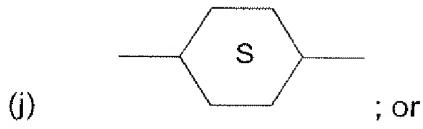
(c) a bicyclic amine containing five to twelve carbon atoms, either bridged or fused and optionally substituted with 1-3 substituents independently selected from R⁴; or



Z¹ and G in combination may be

W is

- (a) $-CH_2-$;
- (b) $-CH=CH-$;
- (c) $-O-$;
- (d) $-NR^2-$;
- (e) $-S(O)_n-$;
- (f) $\begin{array}{c} O \\ \parallel \\ -C- \end{array}$;
- (g) $-CR^2(OH)-$;
- (h) $-CONR^2-$;
- (i) $-NR^2CO-$;



(k) $-\text{C}\equiv\text{C}-$;

R is hydrogen or C₁-C₆ alkyl;

R² and R³ are independently

- (a) hydrogen; or
- (b) C₁-C₄ alkyl;

R⁴ is

- (a) hydrogen;
- (b) halogen;
- (c) C₁-C₆ alkyl;
- (d) C₁-C₄ alkoxy;
- (e) C₁-C₄ acyloxy;
- (f) C₁-C₄ alkylthio;
- (g) C₁-C₄ alkylsulfinyl;
- (h) C₁-C₄ alkylsulfonyl;
- (i) hydroxy (C₁-C₄)alkyl;
- (j) aryl (C₁-C₄)alkyl;
- (k) $-\text{CO}_2\text{H}$;
- (l) $-\text{CN}$;
- (m) $-\text{CONHOR}$;
- (n) $-\text{SO}_2\text{NHR}$;
- (o) $-\text{NH}_2$;
- (p) C₁-C₄ alkylamino;
- (q) C₁-C₄ dialkylamino;
- (r) $-\text{NHSO}_2\text{R}$;
- (s) $-\text{NO}_2$;
- (t) -aryl; or
- (u) $-\text{OH}$;

R⁵ and R⁶ are independently C₁-C₈ alkyl or together form a C₃-C₁₀ carbocyclic ring;

R^7 and R^8 are independently

- (a) phenyl;
- (b) a C_3 - C_{10} carbocyclic ring, saturated or unsaturated;
- (c) a C_3 - C_{10} heterocyclic ring containing up to two heteroatoms,

selected from -O-, -N- and -S-;

- (d) H;
- (e) C_1 - C_6 alkyl; or
- (f) form a 3 to 8 membered nitrogen containing ring with R^5 or R^6 ;

R^7 and R^8 in either linear or ring form may optionally be substituted with up to three substituents independently selected from C_1 - C_6 alkyl, halogen, alkoxy, hydroxy and carboxy;

a ring formed by R^7 and R^8 may be optionally fused to a phenyl ring;

e is 0, 1 or 2;

m is 1, 2 or 3;

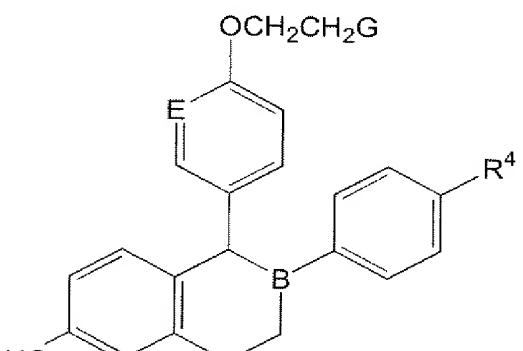
n is 0, 1 or 2;

p is 0, 1, 2 or 3;

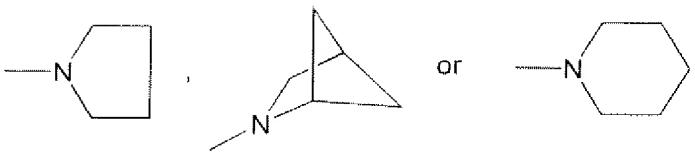
q is 0, 1, 2 or 3;

or an optical or geometric isomer thereof; or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt or prodrug thereof.

55. (previously presented) The method of claim 54 wherein said estrogen agonist / antagonist is a compound of formula (IA):



(IA)



wherein G is

R^4 is H, OH, F, or Cl; and B and E are independently selected from CH and N or an optical or geometric isomer thereof; or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt, or a prodrug thereof.